

Application No.: 09/471,669
Page 2

PATENT

B¹ Cont
This application is a nonprovisional of U.S. Application No. 60/114,408, filed 12/31/1998, now abandoned, U.S. Application No. 60/119,571 filed 2/10/1999, now abandoned, U.S. Application No. 60/139,172 filed 6/15/99, now abandoned, all of which are hereby incorporated herein by reference in their entireties.

☐ Please amend the paragraph beginning at page 2, line 13 as follows.

B²
This invention is directed to a β -secretase protein and in particular to a purified protein characterized by a specific activity of at least about 1.0×10^5 nM/h/ μ g protein in a MBP-C125sw substrate assay, which is representative β -secretase assay that uses a maltose binding protein fused at the carboxy-terminus to the 125 C-terminus amino acids of APP having the cleavage site of SEQ ID NO: 51 (hereinafter referred to as "MBP-C125sw").

☐ Please amend the paragraph beginning at page 9, line 22 as follows.

B³
The term "fragment," when referring to β -secretase of the invention, means a polypeptide which has an amino acid sequence which is the same as part of but not all of the amino acid sequence of full-length β -secretase polypeptide. In the context of the present invention, the full length β -secretase is generally identified as SEQ ID NO: 2, the ORF of the full-length nucleotide sequence; however, according to a discovery of the invention, the naturally occurring active form is probably one or more N-terminal truncated versions, such as amino acids 46-501, 22-501, 58-501 or 63-501; other active forms are C-terminal truncated forms ending between about amino acids 450 and 452. The numbering system used throughout is based on the numbering of the sequence SEQ ID NO: 2.

☐ Please amend the paragraph beginning at line 21 of page 63 as follows.

B⁴
Recombinant proteins were generated with both the 125 C-terminus amino acids of wild-type APP sequence at the cleavage site (..Val-Lys-Met-Asp-Ala..) (SEQ ID NO: 54) (hereinafter referred to as "MBP-C125 wt") or the "Swedish" double mutation (..Val-Asn-Leu-Asp-Ala..) (SEQ ID NO: 51) (also referred to as "MBP-C125sw"). As shown in FIG. 19, cleavage of the intact MBP-fusion protein results in the generation of a truncated amino-terminal fragment, with the new SW-192 Ab-positive epitope uncovered at the carboxy terminus. This amino-terminal fragment can be recognized on Western blots with the same Ab,